REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 17-30 will be active in the application subsequent to entry of this Amendment.

Counsel notes claims 20, 25 and 26 have been indicated to be allowable. While applicant appreciates this indication of allowance applicant also considers the remaining claims to be allowable as well and request reconsideration of them.

Responses to the various issues raised in the Official Action are addressed below.

Response to 35 USC §112 Rejections

The examiner has objection to the phrase "the strands" in claim 23 as having no antecedent basis in either claims 17 or 21. Since claim 23 does not contain this phrase, the Applicant has assumed this to be a typographical error. Assuming that the examiner is referring to the phrase as used in claim 22, then the applicant submits that there is clear basis for the strands in claim 17; the strands refer to the "fluorescently labelled temperature probe DNA sequence" which "comprises a double stranded region which denatures at any desired predetermined temperature". Clearly "the strands" refer to the double stranded regions of the probe, when denatured. However, the Applicant has amended the claim by introduction of the word "denatured" to further clarify to which strands the claims refer.

Claim 31 has been deleted to obviate the §112 rejection of this claim.

Response to 35 USC §103 Rejections

The examiner has rejected claim 17 (and dependent claims 18, 19, 21-24 and 27-30) as being obvious over Tyagi et al (US 5,925,517) in combination with Livak et al (US 5,736,333).

Tyagi discloses fluorescently labelled probes suitable for detecting a nucleic acid target sequence, particularly in the context of a PCR reaction into which the probe has been added. However, the probe of Tyagi is designed to bind to the product of the PCR reaction and thereby produce a shift in fluorescence that can be used to detect the presence of the target sequence. There is no disclosure in Tyagi of a method of monitoring the temperature of a reaction whereby a probe is added with the explicit purpose of monitoring the temperature, and which produces a change in signal when the target temperature is reached.

The examiner acknowledges that there is no teaching in Tyagi that the change in fluorescence when the probe denatures can be used to determine the temperature of the reaction. In fact, the probes described by Tyagi would not work in the method of the present invention. According to the disclosure at *column 13 lines 21-32* the melting temperature of the probe

> *"must be above the assay temperature, so that the probe does not open before the target complement sequence hybridizes to a target, and yet sufficiently below the melting temperature of the hybrid...of the target complement sequence with the with the target sequence to ensure the proper probe functioning"*

Clearly, this would teach the skilled person that, in determining the quantity of amplification product, the probe must be designed within such a narrow specification to avoid false readings and cannot teach the skilled person that by designing a probe which melts at any specific predetermined temperature allows for a method whereby the temperature of the reaction mixture can be monitored separately to, or in conjunction with, the amplification monitoring that was routine in the art at the time of the present invention and exemplified by Tyagi.

There would be no motivation for the skilled person to design probes which denature at any specific temperature based on the teachings of Tyagi alone. Nor is this motivation provided by the teachings of Livak. In fact, Livak teaches away from the present invention because it describes probes, which are designed to accurately quantify the amount of amplification product by measuring a ratio fluorescence emitted by separate probes in order to remove systemic variability (see column 9 lines 15-24). Further, Livak describes the use of a traditional temperature probe to monitor the temperature of a wide range of reaction vessels. Thus the apparatus and method provided by Livak are subject to the same problems that the present invention seeks to overcome, namely to avoid using physical temperature probes

The concept of using a chemical means as a temperature probe, or that the chemical means could be a fluorescently labelled polynucleotide sequence which is designed to melt at any predetermined temperature is not disclosed in Livak. If the skilled person was motivated to combine the teachings of Livak with Tyagi, he would simply be provided with a more accurate

method of quantifying amplification product and would only be motivated to use an external temperature probe.

The Applicant submits that there is no teaching in Livak and Tyagi combined to provide a method of monitoring the temperature of a reaction and thus, we believe that the present invention, as defined by claims 17 to 30, is not obvious over the teaching of Tyagi when taken either alone or in combination with that of Livak.

Reconsideration and allowance are solicited. Should the examiner require further information please contact the undersigned.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
Arthur R. Crawford
Reg. No. 25,327

ARC:eaw
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100